UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/566,409	08/24/2006	Jeffrey A. Ledbetter	910180.40102USPC	3616

500 7590 02/20/2009
SEED INTELLECTUAL PROPERTY LAW GROUP PLLC
701 FIFTH AVE
SUITE 5400
SEATTLE, WA 98104

EXAMINER	
BRISTOL, LYNN ANNE	

ART UNIT	PAPER NUMBER
1643	

MAIL DATE	DELIVERY MODE
02/20/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/566,409	LEDBETTER ET AL.	
	Examiner	Art Unit	
	LYNN BRISTOL	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *1* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 November 2008*.

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *414-445* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *414-445* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)

2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.

4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .

5) ☐ Notice of Informal Patent Application

6) ☐ Other: _____.

DETAILED ACTION

1. Claims 414-445 are all the pending claims for this application.

2. Claims 1-413 were cancelled and new Claims 414-445 were added in the Reply of 11/25/08.

3. New Claims 414-445 raise new issues for consideration in view of meeting the requirements for unity of invention therefore the Office Action of 7/10/08 is *vacated*.

Priority

4. Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 119(e) or 120 as follows:

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

The disclosure of the prior-filed applications, Provisional Application No. 60/367,358 (filed 1/17/01; converted from non-provisional Application No. 09/756,208); Application No. 10/530, 530 (filed 1/17/02) and Application No. 10/627,556 (filed

7/26/03), fails to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application.

None of the priority documents contemplates generating a fusion protein comprising an altered immunoglobulin hinge where a proline residue is mutated much less to a serine. The instant pending claims are accorded a priority date of 12/24/03 for purposes of determining unity of invention (and applying prior art).

Lack of Unity: Restriction

5. Restriction is required under 35 U.S.C. 121 and 372.

The claims of the present application relate to a fusion protein comprising an immunoglobulin binding domain that binds CD20, and altered hinge where a proline is mutated and an N-terminal truncated immunoglobulin heavy chain constant region.

In assessing whether the requirements of unity of invention of an application are met, identification of the technical features that each solution to a technical problem contributes over the prior art (special technical features) must be made. If then a technical relationship between the solutions, involving one or more of the same technical features, can be recognized, the requirements of unity of invention are said to be met.

A fusion protein comprising an immunoglobulin binding domain that binds CD20, and altered hinge where a proline is mutated and an N-terminal truncated immunoglobulin heavy chain constant region was known in the art prior to the priority date (12/24/03) of the instant claims. For example Schilling (US 20050084933;

published April 21, 2005; filed December 18, 2003) teaches a fusion protein, such as CTLA4Ig or mutant, including a portion of the Ig constant region, including human or non-human primate Ig constant regions and the Ig moiety can also hinge modifications which include the proline at position +148 substituted with a serine. Ledbetter et al. (USPN 6623940; published September 23, 2003) teaches fusion proteins recognizing or associated with non-CD molecules such as CTLA4 and the CD20 antigen as a target where the fusions contain sequence changes, i.e. cysteine residues, which mutate the hinge disulfides to serines (HS1). For example, monomer mutant 1 (mut1) (HS2) contains a proline to serine change at residue 238 in the CH2 domain; and monomer mut2 (HS3) is mutated for several residues (234-238) in this region of CH2. Dimer mut1 (DM1) contains wildtype sequences in the hinge region of the Fc domain, but is also mutant for CH2 sequences encoding residues 234-238. Schilling in view of Ledbetter appreciate and teach modifying fusion proteins that recognize CD20 by changing hinge residues to include changing proline residues.

6. This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. The resulting separate inventions, as presently identified, have been grouped according to the order in which they have been claimed.

In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

Group I, claim(s) 414-439, drawn to a fusion protein comprising an immunoglobulin binding domain that binds CD20, and altered hinge where a proline is

mutated and an N-terminal truncated immunoglobulin heavy chain constant region; a pharmaceutical composition thereof.

Group II, claim(s) 440-442, drawn to a method of treating a B-cell disorder with a fusion protein of Claim 414 comprising administering an effective amount to a patient.

Group III, claim(s) 443-445, drawn to a polynucleotide encoding a fusion protein of Claim 414; a vector comprising the polynucleotide; a host transfected with the vector.

7. As no technical features can be distinguished which, in light of the prior art, could be regarded as special technical features on which a unifying concept could be based, there is no single inventive concept underlying the plurality of claimed inventions.

8. The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and the product claims are subsequently found allowable, withdrawn process claims that depend from or otherwise require all the limitations of the allowable product claim will be considered for rejoinder. <u>All</u> claims directed to a nonelected process invention must require all the limitations of an allowable product claim for that process invention to be rejoined.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103 and 112. Until all claims to the elected product are found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowable product claim will not be rejoined. See MPEP § 821.04(b). Additionally, in order to retain the right to rejoinder in accordance with the above policy, applicant is advised that the process claims should be amended during prosecution to require the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder**. Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

9. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim

remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

10. This application contains claims directed to more than one species of the generic invention. These species are deemed to lack unity of invention because they are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for more than one species to be examined, the appropriate additional examination fees must be paid. The species (element (ii) of Claim 431 for the substituted cysteines in the hinge) are as follows:

(a) the first cysteine is substituted with serine
(b) the second cysteine is substituted with serine
(c) the third cysteine is substituted with serine
(d) the first and second cysteines are each substituted with serine
(e) the first and third cysteines are each substituted with serine
(f) the second and third cysteines are each substituted with serine
(g) the first second and third cysteines are each substituted with serine

The claims are deemed to correspond to the species listed above in the following manner: Claim 414 is directed to the fusion protein comprising the altered hinge with a praline mutation.

The following claim(s) are generic: Claim 414, 440 and 443.

The species listed above do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, the species lack the same or corresponding special technical features for the following reasons:

Each of the specifically claimed fusion proteins of the specifically recited binding domain, altered hinge and truncated heavy chain constant region lack unity of invention because the amino acid sequences for each fusion protein have no substantial structural similarities although they have a common utility, i.e. binding CD20. *In re Harnisch*, 631 F.2d 716, 206 USPQ 300(CCPA 1980); and *Ex parte Hozumi*, 3 USPQ2d 1059 (Bd. Pat. App. & Int. 1984).

Furthermore, there are approximately eight different databases that accompany the results of a search of species and each result set from a particular database must be carefully considered. Hence, the search of two different fusion proteins, would require extensive searching and review.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed invention for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable.

Applicant is advised that a reply to this requirement must include an identification of the invention that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

11. This application contains claims directed to more than one species of the generic invention. These species are deemed to lack unity of invention because they are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for more than one species to be examined, the appropriate additional examination fees must be paid. The species (fusion protein of Claims 435-437) are as follows:

SEQ ID NO:135 (2H7 scFv (CSS-S)H WCH2 WCH3), wherein proline at position 283 is substituted with serine,
SEQ ID NO:137 (2H7 scFv (SCS-S)H WCH2 WCH3), wherein proline at position 283 is substituted with serine,
SEQ ID NO:166 (2H7 scFv (CSC-S)H WCH2 WCH3), wherein proline at position 283 is substituted with serine,
SEQ ID NO:372 (2H7 scFv VHL11S (CSS-S)H WCH2 WCH3),
SEQ ID NO:246 (2H7 scFv VH L11S (CSC-S)H WCH2 WCH3),
SEQ ID NO:370 (2H7 scFv VH L11S (SSS-S)H WCH2 WCH3),
SEQ ID NO:268 (2H7 scFv VH L11S (CSS-S)H K322S CH2 WCH3),
SEQ ID NO:276 (2H7 scFv VH L11S (CSS-S)H P331S CH2 WCH3)

The claims are deemed to correspond to the species listed above in the following manner: Claim 414 encompass each of the fusion proteins.

The following claim(s) are generic: Claims 414, 440 and 443.

The species listed above do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, the species lack the same or corresponding special technical features for the following reasons:

Each of the specifically claimed fusion proteins comprises specifically recited amino acid sequences or as defined by art-recognized name lack unity of invention because the amino acid sequences have no substantial structural similarities although they have a common utility, i.e. binding CD20. *In re Harnisch*, 631 F.2d 716, 206 USPQ 300(CCPA 1980); and *Ex parte Hozumi*, 3 USPQ2d 1059 (Bd. Pat. App. & Int. 1984).

Furthermore, there are approximately eight different databases that accompany the results of a search of one discrete amino acid or nucleotide sequence and each result set from a particular database must be carefully considered. Hence, the search of two different amino acid sequences, and different amino acid segments in the databases would require extensive searching and review.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed invention for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable.

Applicant is advised that a reply to this requirement must include an identification of the invention that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

12. This application contains claims directed to more than one species of the generic invention. These species are deemed to lack unity of invention because they are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for more than one species to be examined, the appropriate additional examination fees must be paid. The species (B-cell disorder in Claims 441 and 442) are as follows:

B-cell lymphoma
chronic lymphocytic leukemia
rheumatoid arthritis,
systemic lupus erythematosus,
type I diabetes mellitus,
multiple sclerosis,
immune thrombocytopenic purpura,
psoriasis,
inflammatory bowel disease,
Crohn's disease
ulcerative colitis

The claims are deemed to correspond to the species listed above in the following manner: Claim 440 is drawn to a method of treating a B-cell disorder where the disorders are listed as species members in a Markush group of Claim 441 or 442.

The following claim(s) are generic: Claims 414, 440 and 443.

The species listed above do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, the species lack the same or corresponding special technical features for the following reasons:

Each of the specifically claimed disorders lack unity of invention because the species can originate from any number of different cell types (e.g., epithelial, mesothelial or endothelial). Also, the disorders being associated with different organs are under the influence of different growth factors, hormones, cytokines, etc. Additionally, numerous studies have shown that receptor density and affinity for different therapeutic biomolecules is highly variable amongst different tissues and organs, in addition to there being differences to the extent to which biomolecules are able to penetrate tissues and organs. This suggests that any method inventions involving

administering a therapeutic in the realm of disorder, would require different routes of administration, dosing, formulation, sensitivity of detection, etc., and that one could not predict biodistribution of the therapeutic agent in a subject much less an outcome of success for treating any species disorder in following the same method steps or conditions. *In re Harnisch*, 631 F.2d 716, 206 USPQ 300(CCPA 1980); and *Ex parte Hozumi*, 3 USPQ2d 1059 (Bd. Pat. App. & Int. 1984).

Applicant is required under 35 U.S.C. 121 to elect a single disclosed invention for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable.

Applicant is advised that a reply to this requirement must include an identification of the invention that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lynn Bristol whose telephone number is 571-272-6883. The examiner can normally be reached on 8:00-4:00, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Lynn A. Bristol/
Partial Signatory Authority